```
### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 02.05.06D

Last logoff:  04jun02 15:35:53
Logon file001 04jun02 16:07:58
KWIC is set to 50.
HILIGHT set on as '*'

File   1:ERIC  1966-2002/May 10
       (c) format only 2002 The Dialog Corporation

      Set  Items  Description
      ---  -----  -----------
Cost is in DialUnits
?b 155
       04jun02 16:08:02 User259876 Session D353.1
            $0.29    0.084 DialUnits File1
     $0.29  Estimated cost File1
     $0.01  TELNET
     $0.30  Estimated cost this search
     $0.30  Estimated total session cost   0.084 DialUnits


File 155:MEDLINE(R)  1966-2002/May W4
*File 155: Daily alerts are now available. This file has
been reloaded. Accession numbers have changed.

      Set  Items  Description
      ---  -----  -----------
?s (neurodegenerative (w) disease) and (gene (w) therapy)
            8466  NEURODEGENERATIVE
         1318427  DISEASE
            1125  NEURODEGENERATIVE(W)DISEASE
          565892  GENE
         1835886  THERAPY
           18053  GENE(W)THERAPY
      S1      21  (NEURODEGENERATIVE (W) DISEASE) AND (GENE (W) THERAPY)
?s s1 and (neurotrophic (w) factor)
              21  S1
            8320  NEUROTROPHIC
          529510  FACTOR
            5279  NEUROTROPHIC(W)FACTOR
      S2       5  S1 AND (NEUROTROPHIC (W) FACTOR)
?s s1 and review
              21  S1
          280792  REVIEW
      S3       5  S1 AND REVIEW
?rd
...completed examining records
      S4       5  RD (unique items)
```

?t s4/3,k/all

4/3,K/1
DIALOG(R)File 155:MEDLINE(R)

10955559 20516035 PMID: 11060707
Apoptosis modulators in the therapy of neurodegenerative diseases.
Deigner H P; Haberkorn U; Kinscherf R
Anatomy and Cell Biology III University of Heidelberg, Germany.
Expert opinion on investigational drugs (ENGLAND) Apr 2000, 9 (4) p747-64, ISSN 1354-3784 Journal Code: 9434197
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Apoptosis is a prerequisite to model the developing nervous system. However, an increased rate of cell death in the adult nervous system underlies *neurodegenerative* *disease* and is a hallmark of multiple sclerosis (MS) Alzheimer's- (AD), Parkinson- (PD), or Huntington's disease (HD). Cell surface receptors (e.g., CD95/APO...

... auspicious gene therapeutical approach for human NGF secretion, which has been shown to protect cholinergic neurones from cell death when implanted in the brain. This *review* summarises and evaluates novel aspects of anti-apoptotic concepts and pharmacological intervention including gene therapeutical approaches currently being proposed or utilised to treat neurodegenerative diseases.
; Anti-Inflammatory Agents, Non-Steroidal--therapeutic use--TU; Cytokines --therapeutic use--TU; *Gene* *Therapy*; Growth Substances--therapeutic use --TU; Neurodegenerative Diseases--pathology--PA; Neurodegenerative Diseases--physiopathology--PP; Oxidative Stress; Protease Inhibitors --therapeutic use--TU

4/3,K/2
DIALOG(R)File 155:MEDLINE(R)

10876028 20435204 PMID: 10978846
Glial cell line-derived neurotrophic factor (GDNF) as a defensive molecule for *neurodegenerative* *disease* : a tribute to the studies of antonia vernadakis on neuronal-glial interactions.
Bohn M C; Kozlowski D A; Connor B
Children's Memorial Institute for Education and Research, Department of Pediatrics, Children's Memorial Hospital, Northwestern University Medical School, Chicago, IL 60613, USA. m-bohn@nwu.edu
International journal of developmental neuroscience : the official journal of the International Society for Developmental Neuroscience (ENGLAND) Nov 2000, 18 (7) p679-84, ISSN 0736-5748 Journal Code: 8401784
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Glial cell line-derived neurotrophic factor (GDNF) as a defensive molecule for *neurodegenerative* *disease* : a tribute to the studies of antonia vernadakis on neuronal-glial interactions.
... cell line-derived neurotrophic factor (GDNF). Delivery of the GDNF gene to rat models of Parkinson's disease suggests a potential clinical use of GDNF *gene* *therapy* for humans with this disease. This *review* article briefly summarizes the history of GDNF and the effects of GDNF gene delivery prior to or after a lesion of the rat nigrostriatal system.

4/3,K/3

DIALOG(R)File 155:MEDLINE(R)

10484827 20003089 PMID: 10529788

The search for neural progenitor cells: prospects for the therapy of *neurodegenerative* *disease*.

Shihabuddin L S; Palmer T D; Gage F H

The Salk Institute for Biological Studies, Laboratory of Genetics, 10010 North Torrey Pines Road, La Jolla, CA 92037, USA. chehabeddine@salk.edu

Molecular medicine today (ENGLAND) Nov 1999, 5 (11) p474-80, ISSN 1357-4310 Journal Code: 9508560

Contract/Grant No.: N01-NS-6-2348; NS; NINDS

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The search for neural progenitor cells: prospects for the therapy of *neurodegenerative* *disease*.

... system (CNS) disease could focus on one or more steps that lead to cell loss. In the past decade, cell therapy and/or ex vivo *gene* *therapy* have emerged as possible strategies for the treatment of neurodegenerative diseases. The ability to grow CNS-derived neural progenitor cells using growth factors has been...

... diseases. Further identification of the molecules that direct the differentiation of adult neural progenitors may allow their activation in vivo to induce self-repair. This *review* addresses the nature, distribution and regulation of neural stem cells and the potential for applying these cells to both structural CNS repair and *gene* *therapy*.

; Adult; Brain--embryology--EM; Brain--growth and development--GD; Brain Tissue Transplantation; Cell Differentiation; Cell Division; Cell Lineage; Cells, Cultured--transplantation--TR; Fetal Tissue Transplantation; *Gene* *Therapy*--methods--MT; Neurons--cytology--CY; Organ Specificity; Rats; Stem Cells--transplantation--TR

4/3,K/4

DIALOG(R)File 155:MEDLINE(R)

09162002 97071953 PMID: 8914798

Multipotent neural progenitor or stem-like cells may be uniquely suited for therapy for some neurodegenerative conditions.

Snyder E Y; Macklis J D

Harvard Medical School, Children's Hospital, Boston, MA, USA.

Clinical neuroscience (New York, N.Y.) (UNITED STATES) 3 (5) p310-6, ISSN 1065-6766 Journal Code: 9315128

Contract/Grant No.: HD28478; HD; NICHD; NS34247; NS; NINDS; NW33852; PHS; +

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

... pharmacologic and genetic interventions. The feasibility of this broadly applicable neural stem cell-based strategy has been demonstrated in a number of murine models of *neurodegenerative* *disease*. The focus of this *review* will be our recent observation of a possible tropism of such cells for neurodegenerative environments.

Descriptors: *Gene* *Therapy*--methods--MT; *Nerve Degeneration--genetics --GE; *Neuroglia--transplantation--TR; *Neurons--transplantation--TR; *Stem Cells--transplantation--TR

4/3,K/5

DIALOG(R)File 155:MEDLINE(R)

09161999 97071950 PMID: 8914795

Advances in the development of herpes simplex virus-based gene transfer vectors for the nervous system.

Fink D J; Ramakrishnan R; Marconi P; Goins W F; Holland T C; Glorioso J C

Department of Molecular Genetics and Biochemistry, University of Pittsburgh School of Medicine, PA, USA.

Clinical neuroscience (New York, N.Y.) (UNITED STATES) 3 (5) p284-91, ISSN 1065-6766 Journal Code: 9315128

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Herpes simplex virus (HSV) is an attractive candidate vector for treatment of nervous system disease by *gene* *therapy*. Here we *review* molecular aspects of the natural biology of HSV as it relates to vector design and application. Although gene transfer and transient expression was readily achieved using first generation replication defective HSV vectors, these vectors did not provide for long-term transgene expression, a prerequisite for effective treatment of *neurodegenerative* *disease*. The principle impediments to effective use of HSV vectors are residual toxicity of non-replicating vectors and the silencing of transgene expression from persisting latent...

Descriptors: *Gene* *Therapy*; *Gene Transfer Techniques; *Genetic Vectors; *Nervous System Diseases--therapy--TH; *Simplexvirus--genetics--GE

?ds

Set	Items	Description
S1	21	(NEURODEGENERATIVE (W) DISEASE) AND (GENE (W) THERAPY)
S2	5	S1 AND (NEUROTROPHIC (W) FACTOR)
S3	5	S1 AND REVIEW
S4	5	RD (unique items)

```
?s s1 and review
            21  S1
        280792  REVIEW
     S5      5  S1 AND REVIEW
?s s1 and (neurotrophin or BDNF)
            21  S1
          2995  NEUROTROPHIN
          2180  BDNF
     S6      1  S1 AND (NEUROTROPHIN OR BDNF)
?t s6/3,k/all
```

6/3,K/1

DIALOG(R)File 155:MEDLINE(R)

09426120 97303966 PMID: 9160251

Prevention of motoneuron death by adenovirus-mediated neurotrophic factors.

Gimenez y Ribotta M; Revah F; Pradier L; Loquet I; Mallet J; Privat A

INSERM U. 336, DPVSN, University of Montpellier, France.

Journal of neuroscience research (UNITED STATES) May 1 1997, 48 (3) p281-5, ISSN 0360-4012 Journal Code: 7600111

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Amyotrophic lateral sclerosis (ALS) is a fatal *neurodegenerative* *disease* characterized by progressive loss of motoneurons, and has no effective treatment. Experimental studies in rodents have shown that motoneurons respond to a variety of molecules including brain-derived neurotrophic factor (*BDNF*). and the glial-cell line-derived neurotrophic factor (GDNF). Here we investigated the neuroprotective effect of these growth factors, encoded by an adenovirus, on the death of axotomized facial motoneurons in newborn rats. We used a new *gene* *therapy* strategy that involves gene transfer to motoneurons by intramuscular injection of an

adenoviral vector, which is retrogradely transported from injected target muscle (Finiels et al.,: NeuroReport 7:373-378, 1995). A significant increased survival of motoneurons was observed in animals pretreated with adenovirus encoding *BDNF* (34.5%, P < 0.05) ou GDNF (41.9%, P < 0.05) 1 week after axotomy. These results indicate that pretreatment with *BDNF* or GDNF, using this therapeutic strategy, is able to prevent the massive death of motoneurons that normally follows axotomy in the neonatal period, opening new...
?ds

Set	Items	Description
S1	21	(NEURODEGENERATIVE (W) DISEASE) AND (GENE (W) THERAPY)
S2	5	S1 AND (NEUROTROPHIC (W) FACTOR)
S3	5	S1 AND REVIEW
S4	5	RD (unique items)
S5	5	S1 AND REVIEW
S6	1	S1 AND (NEUROTROPHIN OR BDNF)

?t s2/3,k/all

2/3,K/1
DIALOG(R)File 155:MEDLINE(R)

12818842 21548870 PMID: 11690619
Sustained delivery of GDNF: towards a treatment for Parkinson's disease.
Zurn A D; Widmer H R; Aebischer P
Division of Surgical Research and Gene Therapy Center, Pavillon 4, CHUV, CH-1011, Lausanne, Switzerland. anne.zurn@chuv.hospvd.ch
Brain research. Brain research reviews (Netherlands) Oct 2001, 36 (2-3) p222-9, ISSN 0165-0173 Journal Code: 8908638
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Parkinson's disease (PD) is a *neurodegenerative* *disease* characterized by the progressive loss of nigral dopaminergic neurons. Although symptomatic therapies to substitute for the missing neurotransmitter dopamine are efficient at the early stages of the disease, the goal is to find alternative therapies which could protect dopaminergic neurons from the degenerative process. We have used two distinct *gene* *therapy* approaches to deliver the neuroprotective molecule glial cell line-derived *neurotrophic* *factor* (GDNF) in animal models of the disease: (i) an encapsulated genetically engineered cell line releasing GDNF (ex vivo *gene* *therapy*); and (ii) a lentiviral vector encoding the GDNF gene (in vivo *gene* *therapy*). Both approaches allowed protection of nigral dopaminergic neurons against lesion-induced cell death in rodent as well as monkey models of PD. Behavioral symptoms were...
Descriptors: Brain Tissue Transplantation--methods--MT; **Gene* *Therapy* --methods--MT; *Genetic Vectors--therapeutic use--TU; *Nerve Tissue Proteins--therapeutic use--TU; *Parkinsonian Disorders--genetics--GE; *Parkinsonian Disorders--therapy--TH; *Substantia Nigra--surgery--SU; Cells, Cultured; Diffusion Chambers, Culture--methods--MT; *Gene* *Therapy* --instrumentation--IS; Nerve Tissue Proteins--genetics--GE; Nerve Tissue Proteins--secretion--SE; Parkinsonian Disorders--physiopathology--PP; Substantia Nigra--pathology--PA; Substantia Nigra--physiopathology--PP
Chemical Name: Genetic Vectors; Nerve Tissue Proteins; glial cell-line derived *neurotrophic* *factor*

2/3,K/2
DIALOG(R)File 155:MEDLINE(R)

10876028 20435204 PMID: 10978846
Glial cell line-derived *neurotrophic* *factor* (GDNF) as a defensive molecule for *neurodegenerative* *disease* : a tribute to the studies of antonia vernadakis on neuronal-glial interactions.

Bohn M C; Kozlowski D A; Connor B
Children's Memorial Institute for Education and Research, Department of Pediatrics, Children's Memorial Hospital, Northwestern University Medical School, Chicago, IL 60613, USA. m-bohn@nwu.edu
International journal of developmental neuroscience : the official journal of the International Society for Developmental Neuroscience (ENGLAND) Nov 2000, 18 (7) p679-84, ISSN 0736-5748 Journal Code: 8401784
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Glial cell line-derived *neurotrophic* *factor* (GDNF) as a defensive molecule for *neurodegenerative* *disease* : a tribute to the studies of antonia vernadakis on neuronal-glial interactions.
Research stemming from interests in neuronal-glial interactions has led to the identification of a number of novel trophic factors, such as the dopaminergic *neurotrophic* *factor* glial cell line-derived *neurotrophic* *factor* (GDNF). Delivery of the GDNF gene to rat models of Parkinson's disease suggests a potential clinical use of GDNF *gene* *therapy* for humans with this disease. This review article briefly summarizes the history of GDNF and the effects of GDNF gene delivery prior to or after...
Chemical Name: Nerve Growth Factors; Nerve Tissue Proteins; glial cell-line derived *neurotrophic* *factor*

2/3,K/3
DIALOG(R)File 155:MEDLINE(R)

10844203 20393182 PMID: 10933972
Parkinson's disease: a *neurodegenerative* *disease* particularly amenable to *gene* *therapy*.
Bohn M C
Children's Memorial Institute for Education and Research, Northwestern University Medical School, Chicago, Illinois 60614, USA. m-bohn@nwu.edu
Molecular therapy : the journal of the American Society of Gene Therapy (UNITED STATES) Jun 2000, 1 (6) p494-6, ISSN 1525-0016 Journal Code: 100890581
Contract/Grant No.: NS31957; NS; NINDS; NS39267; NS; NINDS
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Parkinson's disease: a *neurodegenerative* *disease* particularly amenable to *gene* *therapy*.
Descriptors: *Gene* *Therapy*; *Parkinson Disease--therapy--TH; Brain Stem--physiopathology--PP; Dopamine--genetics--GE; Dopamine--physiology --PH; *Gene* *Therapy*--methods--MT; Nerve Tissue Proteins--genetics--GE; Nerve Tissue Proteins--physiology--PH; Parkinson Disease--genetics--GE; Parkinson Disease--physiopathology--PP; Parkinsonian Disorders--therapy --TH; Prosencephalon...
Chemical Name: Nerve Tissue Proteins; glial cell-line derived *neurotrophic* *factor*; Dopamine

2/3,K/4
DIALOG(R)File 155:MEDLINE(R)

10259966 99233150 PMID: 10218782
Long-term actions of vector-derived nerve growth factor or brain-derived *neurotrophic* *factor* on choline acetyltransferase and Trk receptor levels in the adult rat basal forebrain.
Klein R L; Muir D; King M A; Peel A L; Zolotukhin S; Moller J C; Kruttgen A; Heymach J V; Muzyczka N; Meyer E M

Department of Pharmacology and Therapeutics, University of Florida, Gainesville 32610, USA.
Neuroscience (UNITED STATES) Mar 1999, 90 (3) p815-21, ISSN 0306-4522 Journal Code: 7605074
Contract/Grant No.: GM 35723; GM; NIGMS; HL 53665; HL; NHLBI; HL/DK 50257; HL; NHLBI; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Long-term actions of vector-derived nerve growth factor or brain-derived *neurotrophic* *factor* on choline acetyltransferase and Trk receptor levels in the adult rat basal forebrain.

Trophic factor *gene* *therapy* may provide a rational treatment strategy for *neurodegenerative* *disease* . Recombinant adeno-associated virus vectors, incorporating a neuron-specific promoter driving bicistronic expression of green fluorescent protein and either nerve growth factor or brain-derived *neurotrophic* *factor*, transduced 10,000-15,000 neurons in the medial septum for periods of at least six months. Both cholinergic and non-cholinergic neurons expressed green fluorescent protein. Nerve growth factor and brain-derived *neurotrophic* *factor* vectors produced up to 50% increases in immunohistochemical detection of the acetylcholine-synthesizing enzyme in septal neurons ipsilateral to the injection. Increased levels of this enzyme, choline acetyltransferase, persisted for six months with the brain-derived *neurotrophic* *factor* vector. The nerve growth factor vector increased Trk receptor immunoreactivity in a volume of brain exceeding that of the transduced cells. Counterstaining for the neuronal...

Descriptors: Brain-Derived *Neurotrophic* *Factor*--pharmacology--PD; *Choline O-Acetyltransferase--metabolism--ME; *Nerve Growth Factors--pharmacology--PD; *Prosencephalon--metabolism--ME; *Receptor Protein-Tyrosine Kinases--metabolism--ME; *Receptors, Nerve Growth Factor...; Brain-Derived *Neurotrophic* *Factor*--genetics--GE; Dependovirus--genetics--GE; Gene Expression--physiology--PH; Genetic Vectors; Luminescent Proteins--genetics--GE; Nerve Growth Factors--genetics--GE; Rats; Rats, Sprague-Dawley; Receptor, Ciliary *Neurotrophic* *Factor*; Recombination, Genetic; Time Factors; Transgenes--genetics--GE

Chemical Name: Brain-Derived *Neurotrophic* *Factor*; Genetic Vectors; Luminescent Proteins; Nerve Growth Factors; Receptor, Ciliary *Neurotrophic* *Factor*; Receptors, Nerve Growth Factor; green fluorescent protein; Choline O-Acetyltransferase; Receptor Protein-Tyrosine Kinases

2/3,K/5
DIALOG(R)File 155:MEDLINE(R)

09426120 97303966 PMID: 9160251

Prevention of motoneuron death by adenovirus-mediated neurotrophic factors.

Gimenez y Ribotta M; Revah F; Pradier L; Loquet I; Mallet J; Privat A
INSERM U. 336, DPVSN, University of Montpellier, France.
Journal of neuroscience research (UNITED STATES) May 1 1997, 48 (3) p281-5, ISSN 0360-4012 Journal Code: 7600111
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Amyotrophic lateral sclerosis (ALS) is a fatal *neurodegenerative* *disease* characterized by progressive loss of motoneurons, and has no effective treatment. Experimental studies in rodents have shown that motoneurons respond to a variety of molecules including brain-derived *neurotrophic* *factor* (BDNF). and the glial-cell line-derived *neurotrophic* *factor* (GDNF). Here we investigated the neuroprotective effect of these growth factors, encoded by an adenovirus, on the death of axotomized facial motoneurons in newborn rats. We used a new *gene*

therapy strategy that involves gene transfer to motoneurons by intramuscular injection of an adenoviral vector, which is retrogradely transported from injected target muscle (Finiels et al...
Descriptors: Adenoviridae--genetics--GE; *Brain-Derived *Neurotrophic* *Factor*--genetics--GE; *Genetic Vectors; *Motor Neurons--physiology--PH; *Nerve Tissue Proteins--genetics--GE; *Neuroprotective Agents; Animals, Newborn; Axons--physiology--PH; Brain-Derived *Neurotrophic* *Factor* --pharmacology--PD; Cell Death--drug effects--DE; Denervation; Facial Nerve --cytology--CY; Facial Nerve--enzymology--EN; Gene Transfer Techniques; Motor Neurons--drug effects--DE; Motor...
Chemical Name: Brain-Derived *Neurotrophic* *Factor*; Genetic Vectors; Nerve Tissue Proteins; Neuroprotective Agents; glial cell-line derived *neurotrophic* *factor*; beta-Galactosidase
?ds

Set	Items	Description
S1	21	(NEURODEGENERATIVE (W) DISEASE) AND (GENE (W) THERAPY)
S2	5	S1 AND (NEUROTROPHIC (W) FACTOR)
S3	5	S1 AND REVIEW
S4	5	RD (unique items)
S5	5	S1 AND REVIEW
S6	1	S1 AND (NEUROTROPHIN OR BDNF)

```
?s (neurodegenerative (w) disease) and (neurotrophic (w) factor)
            8466  NEURODEGENERATIVE
         1318427  DISEASE
            1125  NEURODEGENERATIVE(W)DISEASE
            8320  NEUROTROPHIC
          529510  FACTOR
            5279  NEUROTROPHIC(W)FACTOR
      S7      34  (NEURODEGENERATIVE (W) DISEASE) AND (NEUROTROPHIC (W)
                  FACTOR)
?s s7 and (treatment or therapy)
              34  S7
         1338007  TREATMENT
         1835886  THERAPY
      S8      24  S7 AND (TREATMENT OR THERAPY)
?s s8 and (BDNF)
              24  S8
            2180  BDNF
      S9       5  S8 AND (BDNF)
?t s9/3,k/all
```

9/3,K/1
DIALOG(R)File 155:MEDLINE(R)

11242857 21281592 PMID: 11388410
Malonate-induced cortico-motoneuron death is attenuated by NT-4, but not by *BDNF* or NT-3.
Van Westerlaak M G; Bar P R; Cools A R; Joosten E A
Department of Experimental Neurology, RMI for Neurosciences, Utrecht, The Netherlands.
Neuroreport (England) May 25 2001, 12 (7) p1355-8, ISSN 0959-4965 Journal Code: 9100935
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Malonate-induced cortico-motoneuron death is attenuated by NT-4, but not by *BDNF* or NT-3.
Neurotrophins are promising candidates to slow the progression of amyotrophic lateral sclerosis (ALS), a *neurodegenerative* *disease* in which spinal and cortical motoneurons selectively degenerate. In a long-term in vitro model, malonate-induced toxicity and cell death of motoneurons have been demonstrated. Here we studied the neuroprotective effect of *BDNF*, NT-3, and NT-4 on the cell death of cortical motoneurons

in an organotypic culture model after chronic mitochondrial inhibition with malonate. Our data show that NT-4 completely prevents malonate-induced toxicity, whereas *BDNF* or NT-3 had no neuroprotective effect. In clinical trials for ALS, predominantly focussed on the survival of spinal motoneurons, *BDNF* has already been tested with disappointing results; our results suggest that NT-4 may be a better neurotrophin to prevent motoneuron loss.

Descriptors: Motor Cortex--drug effects--DE; *Motor Neurons--drug effects --DE; *Nerve Degeneration--drug *therapy*--DT; *Nerve Growth Factors --pharmacology--PD; *Neuroprotective Agents--pharmacology--PD; *Pyramidal Cells--drug effects--DE; Amyotrophic Lateral Sclerosis--drug *therapy*--DT; Amyotrophic Lateral Sclerosis--metabolism--ME; Amyotrophic Lateral Sclerosis--physiopathology--PP; Animals, Newborn; Brain-Derived *Neurotrophic* *Factor*--pharmacology--PD; Cell Death--drug effects--DE; Cell Death--physiology--PH; Cell Survival--drug effects--DE; Cell Survival--physiology--PH; Cells, Cultured--drug effects--DE...

Chemical Name: Brain-Derived *Neurotrophic* *Factor*; Malonates; Nerve Growth Factors; Neurofilament Proteins; Neuroprotective Agents; Neurotrophin 3; neurotrophin 4; Receptor, trkB

9/3,K/2
DIALOG(R)File 155:MEDLINE(R)

10295897 99280375 PMID: 10350547

Trophic effects of selegiline on cultured dopaminergic neurons.

Kontkanen O; Castren E

A.I. Virtanen Institute and Department of Psychiatry, University of Kuopio, P.O. Box 1627, 70211, Kuopio, Finland.

Brain research (NETHERLANDS) May 22 1999, 829 (1-2) p190-2, ISSN 0006-8993 Journal Code: 0045503

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Trophic effects of the neuroprotective agent selegiline on cultured dopaminergic neurons were investigated and compared with the effects produced by brain derived *neurotrophic* *factor* (*BDNF*). Both treatments increased the total length of TH-positive neurites, but selegiline increased the average length of neuritic branches, whereas *BDNF* increased the formation of new branches. This trophic effect of selegiline may contribute to its action in *neurodegenerative* *disease* *treatment*.
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9/3,K/3
DIALOG(R)File 155:MEDLINE(R)

10289842 99268598 PMID: 10338276

Neuron-enriched second trimester human cultures: growth factor response and in vivo graft survival.

White M G; Hammond R R; Sanders V J; Bonaroti E A; Mehta A P; Wang G; Wiley C A; Achim C L

University of Pittsburgh School of Medicine, Department of Pathology, PA 15213, USA.

Cell transplantation (UNITED STATES) Jan-Feb 1999, 8 (1) p59-73, ISSN 0963-6897 Journal Code: 9208854

Contract/Grant No.: NS33429-01; NS; NINDS; NS35419-01; NS; NINDS; NS53731 ; NS; NINDS

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Grafts of first trimester fetal tissue show limited survival and

integration in the adult CNS. Alternative grafting strategies have been sought for *treatment* of *neurodegenerative* *disease*. We have developed cultures of human second trimester fetal tissues to study neuronal differentiation. Grafted into the SCID mouse striatum, aggregates of these cultures formed neuron-rich xenografts for at least 8 months. We examined the influence of various neurotrophic factors, including basic fibroblast growth factor (bFGF), brain-derived *neurotrophic* *factor* (*BDNF*), transforming growth factor-beta 1 (TGF-beta1), and hepatocyte growth factor (HGF), on the growth and differentiation of neuronal and glial cell populations. *BDNF* promoted the survival and differentiation of second trimester neurons whereas bFGF exhibited a strong proliferative effect on precursors and the astroglial population. Our data suggest that second trimester human fetal cultures contain neuroprogenitor cells that can be directed to the neuronal lineage. This process may be amplified by *treatment* with *BDNF*, which we hypothesize could improve the long-term in vivo survival of neuron-enriched grafts.

9/3,K/4
DIALOG(R)File 155:MEDLINE(R)

09747583 98181736 PMID: 9523590

Structure-activity relationships of conformationally constrained peptide analogues of loop 2 of brain-derived *neurotrophic* *factor*.

O'Leary P D; Hughes R A

Department of Pharmacology, University of Melbourne, Parkville, Victoria, Australia.

Journal of neurochemistry (UNITED STATES) Apr 1998, 70 (4) p1712-21, ISSN 0022-3042 Journal Code: 2985190R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Structure-activity relationships of conformationally constrained peptide analogues of loop 2 of brain-derived *neurotrophic* *factor*.

Brain-derived *neurotrophic* *factor* (*BDNF*) promotes the survival of various neuronal populations and thus shows potential in the *treatment* of *neurodegenerative* *disease*. However, *BDNF* is not pharmacokinetically optimal for use as a therapeutic agent. As a step toward the development of low-molecular-weight *BDNF*-like drugs, we have designed a series of small, conformationally constrained peptides of various sizes using the three-dimensional structure of *BDNF* derived by homology modeling as a template. When tested in cultures of embryonic chick sensory neurons the peptides produced concentration-dependent inhibition of *BDNF*-mediated neuronal survival and caused both a rightward shift and depression of the maximum of the *BDNF* concentration-response curve. The compounds had no effect on the survival response to nerve growth factor and were without intrinsic trophic or toxic effects when...

... With the aid of pharmacodynamic simulations we demonstrated that the inhibitory activity of the active peptides is consistent with them acting as competitive antagonists of *BDNF* for its high-affinity receptor, trkB. An alanine scan of the largest peptide identified several residues important in mediating the inhibitory action of the peptides. We intend to use the data from these studies to develop small peptidic *BDNF*-like agonists.

Descriptors: Brain-Derived *Neurotrophic* *Factor* --analogs and derivatives--AA; *Brain-Derived *Neurotrophic* *Factor*--genetics--GE; *Protein Conformation; Amino Acid Sequence; Brain-Derived *Neurotrophic* *Factor*--physiology--PH; Cell Survival--physiology--PH; Cells, Cultured; Chemistry; Chick Embryo; Computer Simulation; Mice; Models, Molecular; Molecular Sequence Data; Neurons, Afferent--physiology--PH; Structure-Activity...

Chemical Name: Brain-Derived *Neurotrophic* *Factor*

9/3,K/5
DIALOG(R)File 155:MEDLINE(R)

09426120 97303966 PMID: 9160251

Prevention of motoneuron death by adenovirus-mediated neurotrophic factors.

Gimenez y Ribotta M; Revah F; Pradier L; Loquet I; Mallet J; Privat A
INSERM U. 336, DPVSN, University of Montpellier, France.

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Amyotrophic lateral sclerosis (ALS) is a fatal *neurodegenerative* *disease* characterized by progressive loss of motoneurons, and has no effective *treatment* . Experimental studies in rodents have shown that motoneurons respond to a variety of molecules including brain-derived *neurotrophic* *factor* (*BDNF*). and the glial-cell line-derived *neurotrophic* *factor* (GDNF). Here we investigated the neuroprotective effect of these growth factors, encoded by an adenovirus, on the death of axotomized facial motoneurons in newborn rats. We used a new gene *therapy* strategy that involves gene transfer to motoneurons by intramuscular injection of an adenoviral vector, which is retrogradely transported from injected target muscle (Finiels et al.,: NeuroReport 7:373-378, 1995). A significant increased survival of motoneurons was observed in animals pretreated with adenovirus encoding *BDNF* (34.5%, P < 0.05) ou GDNF (41.9%, P < 0.05) 1 week after axotomy. These results indicate that pretreatment with *BDNF* or GDNF, using this therapeutic strategy, is able to prevent the massive death of motoneurons that normally follows axotomy in the neonatal period, opening new...

Descriptors: Adenoviridae--genetics--GE; *Brain-Derived *Neurotrophic* *Factor*--genetics--GE; *Genetic Vectors; *Motor Neurons--physiology--PH; *Nerve Tissue Proteins--genetics--GE; *Neuroprotective Agents; Animals, Newborn; Axons--physiology--PH; Brain-Derived *Neurotrophic* *Factor* --pharmacology--PD; Cell Death--drug effects--DE; Denervation; Facial Nerve --cytology--CY; Facial Nerve--enzymology--EN; Gene Transfer Techniques; Motor Neurons--drug effects--DE; Motor...
Chemical Name: Brain-Derived *Neurotrophic* *Factor*; Genetic Vectors; Nerve Tissue Proteins; Neuroprotective Agents; glial cell-line derived *neurotrophic* *factor*; beta-Galactosidase

?ds

Set	Items	Description
S1	21	(NEURODEGENERATIVE (W) DISEASE) AND (GENE (W) THERAPY)
S2	5	S1 AND (NEUROTROPHIC (W) FACTOR)
S3	5	S1 AND REVIEW
S4	5	RD (unique items)
S5	5	S1 AND REVIEW
S6	1	S1 AND (NEUROTROPHIN OR BDNF)
S7	34	(NEURODEGENERATIVE (W) DISEASE) AND (NEUROTROPHIC (W) FACT-OR)
S8	24	S7 AND (TREATMENT OR THERAPY)
S9	5	S8 AND (BDNF)

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